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ORIGINAL RESEARCH

Physical activity is inversely related to drug consumption in elderly patients with cardiovascular events

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Abstract Elderly patients with cardiovascular events are characterized by high drug consumptions. Whether high drug consumptions are related to physical activity is not known. In order to examine whether physical activity is related to drug consumption in the elderly, patients older than 65 years (n=250) with a recent cardiovascular event were studied. Physical activity was analyzed according to the Physical Activity Scale for the Elderly (PASE) score and related to drug consumption. PASE score was 72.4±45.0 and drug consumption was 8.3±2.2. Elderly patients with greater comorbidity took more drugs (8.7±2.1) and are less active (PASE=64.4±50.6) than patients with Cumulative Illness Rating Scale severity score higher than 1.8 than those with a score lower than 1.8 (76.3±41.4, p<0.05, and 8.0±2.0, p=0.006, respectively). Multivariate analysis correlation confirmed that PASE score is negatively associated with drug consumption (β=−0.149, p=0.031), independently of several variables including comorbidity. Thus, physical activity is inversely related to drug consumption in elderly patients with cardiovascular events. This inverse relationship may be attributable to the high degree of comorbidity observed in elderly patients in whom poor level of physical activity and high drug consumption are predominant.

Keywords Physical activity · Drug consumption · Elderly · Cardiovascular event

Introduction

Epidemiologic studies clearly demonstrate that cardiovascular diseases are the leading cause of morbidity and mortality in most countries [25]. Moreover, a rise in cardiovascular disease mortality rates is expected in developing countries over the next 25 years due to the increase of the aging population [25]. Indeed, the vast majority of people aged ≥65 years is characterized by a condition of comorbidity and disability [6, 32]. Both conditions lead to a frailty state and, therefore, to high drug consumption [5, 29].

Elderly subjects represent 13 % of the US population, but receive 34 % of all drug prescriptions [31]. One recent large survey of community-dwelling subjects showed that more than 90 % of individuals aged ≥65 years took at least one drug weekly, more than 40 % used five or more drugs weekly, and 12 % used ten or more drugs weekly [18]. In the UK, elderly patients take on average two to five prescription medications on a regular basis (4±1), and polypharmacy occurs in 20–50 % of patients [19].

To reduce drug use in the elderly population, several types of interventions and strategies have been tested, including educational interventions (i.e., continuing medical education)

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[28]. However, among other interventions aiming at the reduction of drug consumption, physical activity can be considered a good candidate. In fact, cardiorespiratory fitness (at least 30 min or more of moderate-intensity physical activity daily) appears as the strongest prognostic marker in persons with and without cardiovascular diseases [16]. In addition, a growing body of literature suggests that physical activity improves depressive symptoms, dementia, disability, and frailty and reduces mortality in elderly patients [17, 20].

To our knowledge, no data are available on the relationship between physical activity and drug consumption in the elderly. Thus, the aim of our study was to assess whether the degree of physical activity was associated with the number of drugs assumed in the elderly population undergoing a cardiac rehabilitation program after a cardiovascular event.

Methods

Study population

The study enrolled 250 elderly (≥65 years) consecutive patients admitted after cardiac surgery between January 2008 and July 2009 to the Division of Cardiac Rehabilitation. The study received full ethical approval from the "Research Ethics Committee." All participants signed an informed consent form, and the institutional review boards of all participating institutions approved the study. The demographic and clinical variables of these patients were obtained at entry in the Division of Cardiac Rehabilitation Center. The following data were collected: age, sex, type of cardiac surgery (coronary artery bypass grafting—CABG or valve surgery), off-pump CABG, presence of coronary artery disease (CAD), chronic heart failure (CHF), previous stroke, chronic obstructive pulmonary disease (COPD), diabetes, and renal failure (creatinine level≥2.0 mg/dl). The total number of drug and the type of drug used were assessed at entry.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all patients for inclusion in the study.

Comprehensive geriatric multidimensional evaluation

Patients underwent a comprehensive geriatric multidimensional evaluation within the third day after admission, which included cognitive function evaluation with the Mini Mental State Examination [24] and evaluation of depressive symptoms with the Geriatric Depression Scale [36]. Disability was assessed by means of the Barthel Index, which evaluates a patient's self-care abilities in ten areas, including bowel and bladder control. The patient is scored from 0 to 15 points in various categories depending on his or her need for help, such as in feeding, bathing, dressing, and walking. Total scores range from 0 to 100, with higher scores indicating a greater degree of independence [9]. The 6-min walking test (6MWT) was performed on the second day after hospital admission in all patients and, in any case, within the first week after hospitalization. Patients were instructed to walk as far as possible along a 40-m straight, flat hospital corridor in 6 min [22]. The test was symptom-limited, so patients who became symptomatic (e.g., angina, severe dyspnea, dizziness, and musculoskeletal pain) were told to stop walking and restart when possible. Of the 250 enrolled patients, 24 (9.6 %) were not able to perform the 6-min walking test. These patients were not excluded, but their score was considered equal to 0. The test was supervised by a physical therapist who encouraged the patients in a standardized fashion at regular intervals. The total distance walked was measured to the nearest meter and recorded. The results of the 6MWT are given as absolute values in meters. Severity of comorbid conditions was evaluated by means of the Cumulative Illness Rating Scale (CIRS) [10]. The CIRS is accepted to be a valid and reliable measure of multiple morbidities. The index quantifies the burden of chronic illness in a patient by taking into account the number and severity of different illnesses across 14 anatomical and physiological systems. Each condition identified was rated on a scale from 0 to 4, where 0 indicates that there is no problem affecting that system, 1 indicates a mild current problem or a past significant problem, 2 indicates a moderate problem requiring first-line therapy, 3 indicates a severe problem that may be associated with significant disability or is hard to control, and 4 indicates an extremely severe problem, organ failure, or severe functional impairment. Equilibrium and risk of fall were measured with the Tinetti Scale [33]. Social support evaluation with Social Support Assessment was scored from 4 (subjects with the highest support) to 1 (subjects with the lowest support) [23]. Neuro-sensitive evaluation with hearing impairment was scored from 1 (no hearing problem) to 4 (total deafness) [4]. Visual impairment was scored from 1 (no visual impairment) to 4 (blindness) [7]. Urinary and fecal incontinence was also assessed. Usual physical activity performed before cardiac surgery was assessed by means of the Physical Activity Scale for the Elderly (PASE) [35] on the second day after hospital admission in all patients and, in any case, within the first week. The PASE is a brief (5 min) and easily scored survey designed specifically to assess physical activity in epidemiologic studies of persons aged 65 years and older. The PASE assesses physical activity over a 1-week time frame. Participation in leisure activities, including walking outside the home; light, moderate, and strenuous sport and recreation; and muscle strengthening were recorded as never, seldom (1–2 days/week), sometimes (3–4 days/week), and often (5–7 days/week). Duration was categorized as <1 h, between 1 and 2 h, 2–4 h, or more than 4 h. Paid or unpaid work, other than work that involves mostly sitting activity, was

recorded in total hours per week. Housework (light and heavy), lawn work/yard care, home repair, outdoor gardening, and caring for others are recorded as yes/no. Frequency and duration of household activities were not requested. The total PASE score was computed by multiplying the amount of time spent in each activity (hours/week) or participation (yes/no) in an activity by the empirically derived item weights and summing over all activities.

Measure of outcomes

Each active ingredient was considered as a drug; the total number of drugs was evaluated at entry to the Division of Cardiac Rehabilitation. We measured specifically the use of β-blockers (bisoprolol, atenolol, sotalol), digoxin, diuretic, ACE inhibitors, angiotensin receptor inhibitors, nitrates, alpha-blockers, amiodaron, dihidropiridines, diltiazem, verapamil, metformin, glibenclamide, repanglide, insulin, ASA, warfarin, steroids, theophylline, and statins. Drugs consumed over 20 % were reported in Table 1. Other drugs were counted and assessed as total number of drugs.

Statistical analysis

Continuous variables are expressed as the mean±SD. Categorical data are expressed as frequencies and percentages. Univariate analysis (ANOVA) examined the differences in drug use in patients with and without CABG, off-pump CABG, valve surgery, heart failure, CAD, stroke, COPD, diabetes, and renal failure. Univariate regression analysis was used to find a correlation among the number of drugs used and other variables such as age, female sex, MMSE and GDS scores, CIRS score, Barthel Index, 6MWT, PASE, CABG, Op-CABG, valve surgery, CAD, CHF, stroke, COPD, diabetes, and renal failure. Multiple linear regressions among the number of drugs used and variables were found significant at univariate analysis. CIRS was also included into the multivariate regression model as a potential confounder.

All statistical analyses were performed with SPSS software (version 15.0, SPSS Inc., Chicago, IL). A value of $p < 0.05$ was considered statistically significant.

Results

The sample consisted of 250 elderly patients (mean age=73.3 ±4.8 years, range=65–89 years); 120 (48.0 %) were women. One hundred seventy (68 %) underwent cardiac surgery for CABG, 24 patients (9.6 %) had CABG and valve replacement (n=20 aorta valve, n=4 mitral valve), while 56 (22.4 %) had valve replacement (n=38 aorta, n=16 mitral valve replacement). In two patients, both valves were replaced. Off-pump CABG was used in 152 (89.4 %) patients.

Table 1 Baseline characteristics of the 250 patients enrolled in the study

Age (years±SD)	73.3±4.8
Female sex, *n* (%)	120 (48.0)
BMI (kg/m^2)	27.5±5.7
Waist circumference (cm)	103.7±11.5
CABG, *n* (%)	194 (77.6)
Valve surgery, *n* (%)	80 (32.0)
Off-pump CABG, *n* (%)	152 (60.8)
Geriatric multidimensional evaluation	
MMSE (score)	23.3±4.9
GDS (score)	3.9 ±2.5
Tinetti score	9.3±4.3
Visual impairment, *n* (%)	103 (41.2)
Hearing impairment, *n* (%)	44 (17.6)
Social support score	5.6±2.6
PASE	72.4±45.0
Barthel Index	74.0±21.5
6-min walking test	190.9±95.5
Comorbidities	
CIRS severity score	1.8±0.4
CHF, *n* (%)	10 (4.0)
CAD, *n* (%)	202 (80.8)
Stroke, *n* (%)	30 (12.0)
COPD, *n* (%)	106 (42.4)
Diabetes, *n* (%)	142 (56.8)
Renal failure, *n* (%)	34 (13.6)
Drug consumption	
Total drugs used	8.3±2.2
Diuretic, *n* (%)	223 (89.2)
ASA, *n* (%)	178 (71.2)
ACE inhibitors, *n* (%)	144 (57.6)
Statins, *n* (%)	136 (54.4)
Bisoprolol, *n* (%)	110 (44.0)
Amiodaron, *n* (%)	73 (29.2)
Carvedilol, *n* (%)	66 (26.4)
Steroids, *n* (%)	66 (26.4)
Metformin, *n* (%)	65 (26.0)
Warfarin, *n* (%)	52 (20.8)
Insulin, *n* (%)	51 (20.4)
Nitrates, *n* (%)	51 (20.4)

CABG coronary artery bypass grafting, *PASE* Physical Activity Scale for the Elderly, *CIRS* Cumulative Index Rating Scale, *CAD* coronary artery disease, *COPD* chronic obstructive pulmonary disease

Baseline measurements, geriatric multidimensional evaluation, comorbidities, and drug consumption are presented in Table 1. Prevalence of comorbidity was high in this population considering the 80.8 % prevalence of CAD, 12.0 % of stroke, 42.4 % of COPD, 56.8 % of diabetes, 4 % of CHF, and 13.6 % of renal failure. CIRS severity

score was 1.8±0.4, but 33.6 % had a CIRS severity score >1.8. PASE score was 72.4±45.0 (range=0–192), Barthel Index was 74.0±21.5 (range=0–100), while 6MWT was 190.9±95.5 m (range=0–401). Mean drug consumption was 8.3±2.2 (range=4–14). The highest drug consumption was diuretic (89.2 %), followed by salicylate (71.2 %) and angiotensin-converting enzyme inhibitors (57.6 %; Table 1). Moreover, in elderly patients with CIRS severity score higher than 1.8, the PASE score was lower (64.4±50.6) and drug consumption higher (8.7±2.1) than those with CIRS severity score lower than 1.8 (76.3±41.4, $p<0.05$; 8.0±2.0, $p=0.006$, respectively).

Linear regression analysis demonstrates that age and GDS score were positively while PASE, Barthel Index, and 6MWT were negatively correlated with drug consumption (Table 2). When the PASE score is plotted with drug consumption, a significant inverse linear relation was observed ($y=-8.4+146.7x$, $r=0.38$, $p<0.001$; Fig. 1). Accordingly, multivariate linear regression confirmed that age, GDS score, and renal failure are positively associated while, more importantly, the PASE score is negatively, and more importantly, independently associated with drug consumption, independently of CIRS severity (Table 2).

Table 2 Univariate and multivariate linear regression on drug consumption

Variable	Univariate		Multivariate	
	β	p	β	p
Age	0.176	0.005	0.163	0.031
Sex (female)	−0.021	0.739	–	–
GDS	0.301	0.000	0.254	0.000
PASE	−0.219	0.000	−0.150	0.031
Barthel Index	−0.143	0.024	0.053	0.536
6MWT	−0.153	0.016	0.041	0.636
CIRS	0.099	0.118	0.095	0.159
MMSE	−0.104	0.111	–	–
CABG	0.164	0.009	0.089	0.370
OPCABG	0.076	0.232	–	–
Valve surgery	−0.116	0.066	–	–
CHF	−0.044	0.487	–	–
CAD	0.173	0.006	0.092	0.336
Stroke	0.023	0.713	–	–
COPD	0.151	0.017	0.051	0.457
Diabetes	0.205	0.001	0.090	0.165
Renal failure	0.212	0.001	0.160	0.016

GDS Geriatric Depression Scale, *PASE* Physical Activity Scale for the Elderly, *6MWT* 6-min walking test, *CABG* coronary artery bypass grafting, *CAD* coronary artery disease, *COPD* chronic obstructive pulmonary disease

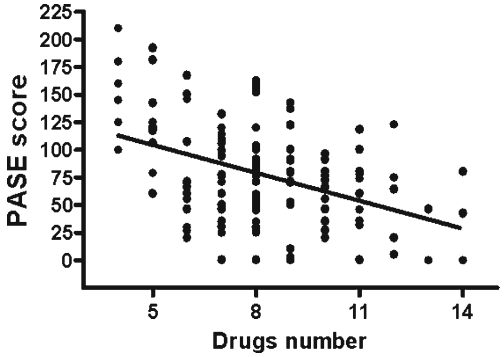

Fig. 1 Linear correlation between physical activity (PASE score) and number of drug consumption in elderly patients with cardiovascular events

Discussion

Our study demonstrates that physical activity is inversely related to drug consumption in elderly subjects with cardiovascular events undergoing cardiac surgery. These results demonstrate that physical activity is inversely associated independently with several variables, including comorbidity.

Polypharmacy in the elderly

Surveys of community-based elderly patients indicate that two to nine prescription medications on average are taken per day [15]. It has been found that 57 % of US women aged ≥65 years took five or more prescription medications, while 12 % took ten or more medications [18]. Similarly, a large study in Europe found that 51 % of patients took six or more medications per day [13]. Accordingly, in our study, the number of drugs used was 8.3±2.2. It should also underline the types of medications that are being consumed. A large national survey found that the most common drugs used in non-institutionalized patients were estrogen products, levothyroxine, hydrochlorothiazide, atorvastatin, and lisinopril [18], while cardiovascular agents, antibiotics, diuretics, opioids, and antihyperlipidemics were the most frequently used drugs in Medicare patients [14]. Similarly, in our sample, diuretics, followed by salicylate and angiotensin-converting enzyme inhibitors, were the drugs more commonly used.

Many consequences may be associated with polypharmacy. Patients are at an increased risk of having an adverse drug reaction (ADR), geriatric syndromes, and morbidity/mortality. The risk of ADRs may increase with increased number of drugs taken and with age-related pharmacodynamic alterations [12]. ADRs, defined as noxious and unintended reactions which occur at dosages normally used in humans for prophylaxis, diagnosis, or therapy, have been reported to occur in 5–35 % of outpatients and account for 12 % of hospital admissions in older patients [14, 15, 26]. More importantly, the risk of ADRs is strongly associated with multiple comorbidities [15], as

confirmed by our results. Polypharmacy in the elderly has also been associated with geriatric syndrome as a cognitive impairment [21] and falls [2]. In our cohort, elderly patients, together with high drug consumption, were characterized by cognitive impairment (MMSE<24). Finally, polypharmacy has been associated with a decline of physical and instrumental activities of daily living [8]. Accordingly, our elderly patients presented a Barthel Index<75.

Interventions to reduce polypharmacy in the elderly

Risk factors of polypharmacy have been identified and classified into three groups: demographic (increased age, white race, and education); health status (depression, hypertension, anemia, asthma, angina, diverticulosis, osteoarthritis, gout, and diabetes mellitus); and access to health care (number of health care visits, supplemental insurance, and multiple providers) [15]. In particular, pharmacodynamic and pharmacokinetic alterations with advancing age have been observed [12]. In our sample, drug consumption was inversely related to physical activity in univariate analysis. More importantly, an inverse relationship was confirmed at multivariate analysis independently by several variables, including diseases highly prevalent in the elderly (i.e., COPD and diabetes).

In addition, the greater comorbidity severity observed in our cohort was associated with elevated drug consumption and low physical activity. The presence of a high degree of comorbidity may surely influence poor physical activity and the large number of drugs consumed. This scenario is worsened by a superimposed aging process which is associated with physiologic changes that naturally predispose older adults to progressive weakening, functional decline, morbidity, disability, poor quality of life, and increased mortality [30]. In contrast, regular exercise provides many physiologic benefits, reduces risk of disease outcomes, and triggers important psychological gains [1, 11]. There is strong evidence that regular physical activity reduces the risk of cardiovascular disease and, therefore, the increased related drug consumption [3]. Because of the preventive effects on cardiovascular disease, physical activity has beneficial effects on functional limitations and health-related quality of life in older adults, such as drug consumption.

Considerations and conclusions

Exercise may exert protective effects on (a) cardiovascular disease by several mechanisms, including lowering cholesterol and decreasing blood pressure and heart rate; (b) immunological system by decreasing the rates of cancer; (c) glucose metabolism by preventing or controlling hyperglycemia and diabetes and, therefore, insulin sensitivity; (d) obesity by increasing basal metabolism and muscle-to-fat ratio; and (e) mental health by decreasing depression and cognitive impairment [34]. In addition, regularly active persons were hospitalized less often than inactive persons, made fewer physician visits, and, more importantly, consumed a lower number of drugs [27]. Although the interpretation of our data would require an experimental design instead of a purely descriptive one, the critical point of our results is the relationship between physical activity and health conditions that might limit participation in physical activity (i.e., the presented findings do not necessarily imply that increasing physical activity reduces drug consumption). Physical inactivity may be both the cause and the effect of disabling disease; therefore, it may be responsible for the high drug consumption. Moreover, the effect of physical activity on drug consumption is independent of comorbidity (i.e., CIRS) in our multivariate model.

We conclude that physical activity is inversely related to drug consumption in elderly patients with cardiovascular events undergoing cardiac surgery. This inverse relationship may be attributable to the high degree of comorbidity observed in elderly subjects with poor level of physical activity.

Conflict of interest F. Cacciatore, F. Mazzella, L. Viati, G. Longobardi, A. Magliocca, C. Basile, L. Guadagno, N. Ferrara, F. Rengo, P. Abete declare that they have no conflict of interest.

Informed consent All subjects were fully informed of the procedures involved and provided written consent.

Ethical statement The study was performed in accordance with the ethical standards laid down in the World Medical Association's Declaration of Helsinki on medical research involving human subjects.

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